REMARKS/ARGUMENTS

GENERAL

Claims 44-50 are pending in this application. Claims 44, has been amended herein. Claims 1-43 and 51-72 have been canceled either previously or in this Amendment. Claims 44-50 stand rejected. The issues raised in the Office Action of February 23, 2010 ("Current Action") are as follows:

* Claims 44-50 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

* Claims 44-50 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification, written description.

* Claims 44-50 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification, enablement.

* Claims 44-46 are rejected under 35 U.S.C. § 102 (e) as being clearly anticipated.

* Claims 44-47, 49, and 50 are rejected under 35 U.S.C. § 102 (b) as being clearly anticipated.

In response, Applicant respectfully traverses the outstanding claim rejections and requests reconsideration and withdrawal in light of the remarks presented herein.

Rejections Under 35 § U.S.C. § 112

Claims 44-50 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite.

The claims have been amended to remove the term "pre-processed" from claim 44 to more clearly claim the invention. As regards TNF-alpha, the invention as claimed and taught is directed to the use of those TNF-alpha molecules that have the same activity as TNF-alpha, e.g., isotypes or mutants of TNF-alpha. For the sake of compact prosecution, the Applicants are willing to amend the specification to make clear that TNF-alpha is limited to TNF-alpha and does not extend to any non-TNF molecules that have overlapping activity (as is common with many cytokines). Applicants respectfully

request the Examiner withdraw the rejection under 35 U.S.C. § 112, 2nd paragraph, indefiniteness.

Claims 44-50 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification, written description.

For the sake of compact prosecution, the Applicants are willing to amend the specification to make clear that TNF-alpha is limited to TNF-alpha molecules and does not extend to any non-TNF molecule that have overlapping activity (as is common with many cytokines). Applicants respectfully request the Examiner withdraw the rejection under 35 U.S.C. § 112, 1st paragraph, written description.

Claims 44-50 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification, enablement.

The claims of the present invention are rejected because other art failed to achieve the present invention. The Current Action argues that Pickl, et al., attempted that which is claimed, and that their failure in an MLR reaction places into question the present invention (Citing Rasmusson v. SmithKline Beecham Corp., 75 USPQ2d 1927, 1302 (CAFC 2005), and in re Wands, 858 F.2d at 737, 8 USPQ2d at 1404). However, Pickl actually teaches that highly purified dendritic cells in a Mixed Lymphocyte Reaction (MLR) in which the T cells are responding to co-stimulation as a result of allogeneic interactions and not from: (1) loading antigen by the antigen presenting cells; or (2) maturation of the dendritic cells in the presence of: antigen, GM-CSF and TNF-alpha. As such, the art cited is not relevant to the present invention. In fact, it is the essence of inventive step to find art that teaches against the present invention, e.g., Pickl and address that which it failed to achieve, the rapid (less than 4 days) maturation of dendritic cells from monocytes using antigen, GM-CSF and TNF-alpha. Applicants respectfully request the Examiner withdraw the rejection under 35 U.S.C. § 112, 1st paragraph, enablement.

Rejections Under 35 U.S.C. § 102

Claims 44-46 are rejected under 35 U.S.C. § 102 (e) as being anticipated by U.S. Patent No. 6,479,286 by Nelson et al. (hereiafter Nelson).

Claims 44-46 are rejected under 35 U.S.C. § 102(e) as being anticipated by Nelson which is said to disclose the claimed invention. Applicant respectfully submits that Nelson to meet the standard of 35 U.S.C. § 102(e) as Nelson fails to teach each and every limitation of the claimed invention. Thus, Nelson does not anticipate any of the claims of the present invention.

Nelson does not identically disclose every element of the claimed invention. See *Corning Glass Works v. Sumitomo Electric*, 9 USPQ 2d 1962, 1965 (Fed. Cir. 1989). A reference that excludes a claimed element, no matter how insubstantial or obvious, is enough to negate anticipation. *Connell v. Sears, Roebuck & Co.*, 220 USPQ 193, 198 (Fed. Cir. 1983).

The Current Action directs the Applicants' attention to claim 3 of Nelson, which is found hereinbelow:

> **3**. The method of claim **1**, further comprising incubating the dendritic cells with TNF-α, thereby generating activated dendritic cells.

Nothing in claim 3, nor the independent claim it depends on (which teaches that the cells are treated with IL-3, "and subsequently" treating the cells with a combination of IL-4 and GM-CSF), includes each and every element of the claimed invention. In fact, there is no teaching in Nelson of the combination of TNF-alpha and GM-CSF, as such the reference does not and cannot anticipate the claimed invention. Furthemore, the Current Action directs the Applicants' attention to Column 15, which teaches that the cells are "transduced" to express antigens internally, presumably for processing and presentation via class I MHC (see Col. 15, ll. 20-21). The present invention includes no such limitations, as the antigen is loaded concurrent with the activation with TNF-alpha and GM-CSF. For these reasons, Nelson does not anticipate the claimed invention.

Applicant respectfully submits that claims 44-46 are not anticipated by Nelson. Nelson does not identically disclose every element of the claimed invention. Applicants respectfully request the Examiner withdraw the rejection under 35 U.S.C. § 102(e).

Claims 44-47, 49, and 50 are rejected under 35 U.S.C. § 102 (b) as being clearly anticipated by Proliferating Dendritic Cell Progenitors in Human Blood, Nikolaus Romani, et al., 1994 (hereinafter Romani).

Claims 44-47, 49, and 50 are rejected under 35 U.S.C. § 102(b) as being anticipated by Romani which is said to disclose the claimed invention. Applicant respectfully submits that Romani to meet the standard of 35 U.S.C. § 102(b) as Romani fails to teach each and every limitation of the claimed invention. Romani does not identically disclose every element of the claimed invention. Thus, Romani does not anticipate any of the claims of the present invention.

Romani is directed to the isolation of dendritic cell precursors in which cord blood cells were expanded using GM-CSF:

> *Cord Blood Mononuclear Cells as a Source for DC Progenitors.* We began with cord blood, since a prior report had shown that 0.5–10^6 enriched (>95%) $CD34^+$ cord blood cells could give rise to 1–2.5 × 10^7 DCs if cultured for 14 d in a combination of GM-CSF and TNF (14). A limitation to this previous protocol was that cord blood only contains 0.9–2.6% $CD34^+$ cells (30). Therefore, we assessed a prior technique with adult mouse blood (11) in which unfractionated cells or MHC class II negative cells, were cultured in GM-CSF. We found that the varying, yet substantial percentage of nucleated erythroid cells in human cord blood was toxic and that these could be removed by panning with antiglycophorin A mAb. We began, then with erythroid-depleted cord blood cells with a low buoyant density (<1.077 g/ml) and plated these at 1–2 × 10^6/ml in 1 ml of standard medium supplemented with GM-CSF (400–800 U/ml) ± TNF (50 U/ml). The wells were fed every other day by aspirating 0.3 ml medium and adding back 0.5 ml medium with cytokines.

Romani then teaches that the addition of TNF-alpha was "not essential" for the development of the DC precursors. Importantly, these cells were not exposed to antigen

during the maturation into precursors of dendritic cells. As such, Romani not only fails to teach each and every element of the claimed invention (concurrent antigen loading), it actually teaches against the claimed invention (TNF-alpha is not essential). In contrast, the present inventors were able to fully mature dendritic cells in only four days by the combination of exposure to antigen, TNF-alpha and GM-CSF. The Current Action then argues that the fractions would, "inherently include" dead or dying cells and hence, the claim is anticipated. First, there is no teaching in Romani that these dead or dying cells are causing an immune response or that those cells are processed and presented. For these reasons, Romani does not anticipate the claimed invention.

Applicants respectfully submit that claims 44-47, 49, and 50 are not anticipated by Romani. Romani does not identically disclose every element of the claimed invention. Applicants respectfully request the Examiner withdraw the rejection under 35 U.S.C. § 102(b).

CONCLUSION

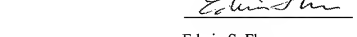
In light of the remarks and arguments presented above, Applicant respectfully submits that the claims in the Application are in condition for allowance. Favorable consideration and allowance of the pending claims 44-50 are therefore respectfully requested.

In view of the above, Applicant believes the pending Application is in condition for allowance. Applicant believes this paper is being filed with all required fees. However, if any additional fee is due, including those for an extension of time please charge any fees required or credit any overpayment to Chalker Flores, LLP's Deposit Account No. 50-4863 during the pendency of this Application pursuant to 37 CFR 1.16 through 1.21 inclusive, and any other section in Title 37 of the Code of Federal Regulations that may regulate fees. If an extension of time is required with this response but is not included, Applicant hereby petitions for a Request for Extension of Time under 37 CFR 1.136(a).

If the Examiner has any questions or comments, or if further clarification is required, it is requested that the Examiner contact the undersigned at the telephone number listed below.

Dated: May 24, 2010.

Respectfully submitted,
CHALKER FLORES, LLP



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